Figure 1

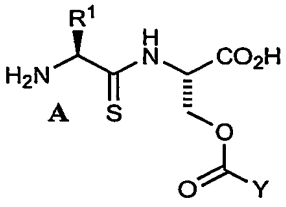
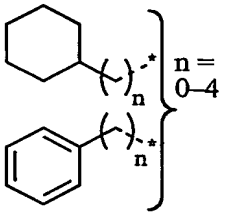
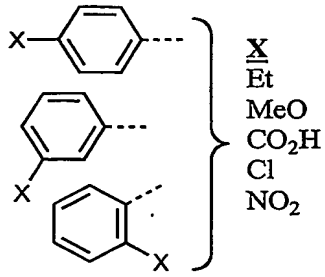
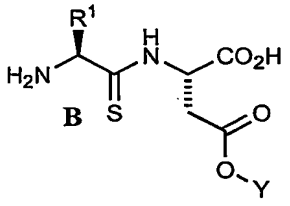
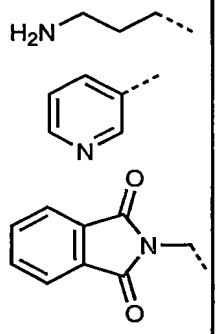
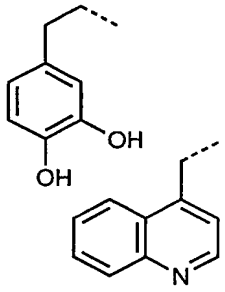
Column A Thiodipeptide core	Column B Y gps (*cf.* drugs)	Column C Y gps (*cf.* drugs)	Column D Side-chain R^1 gps
 	 	 	H Me CH_2Ph $CHMe_2$ CH_2OH CH_2SH CH_2CO_2H CH_2CONH_2 $(CH_2)_4NH_2$
 	 	 	

Figure 2.

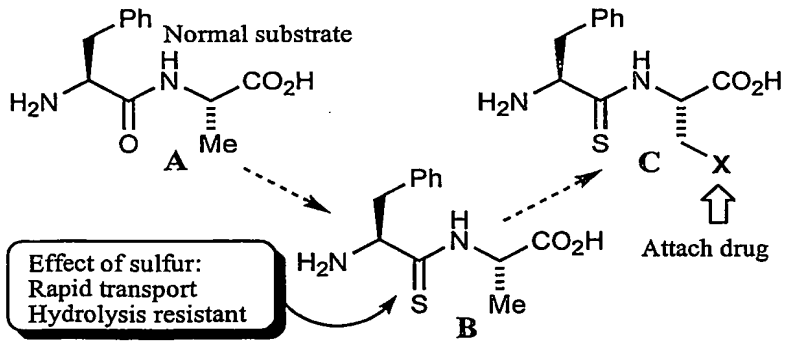


Figure 3

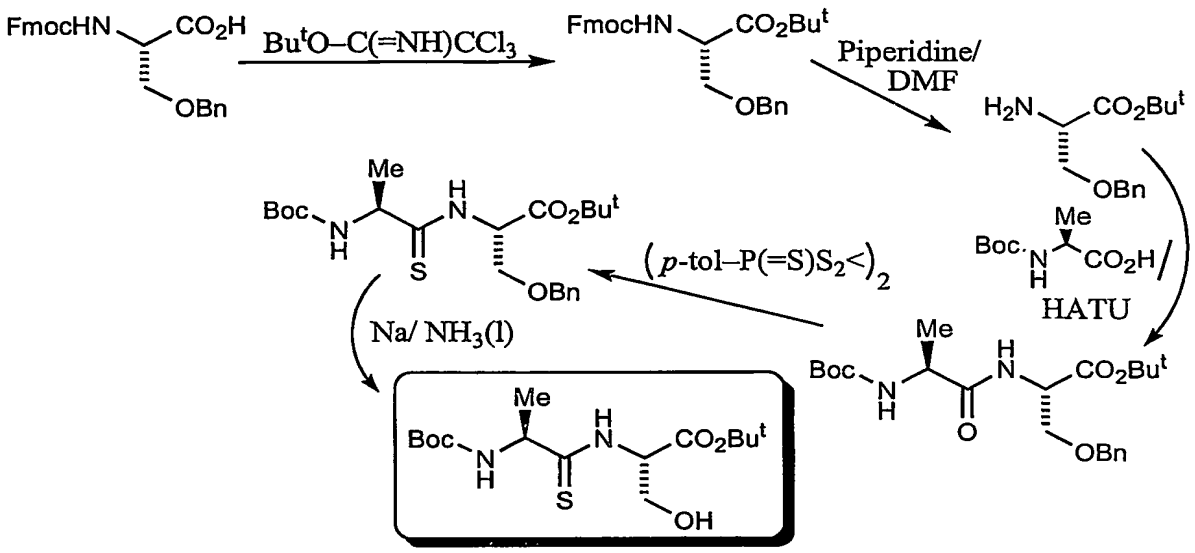


Figure 4

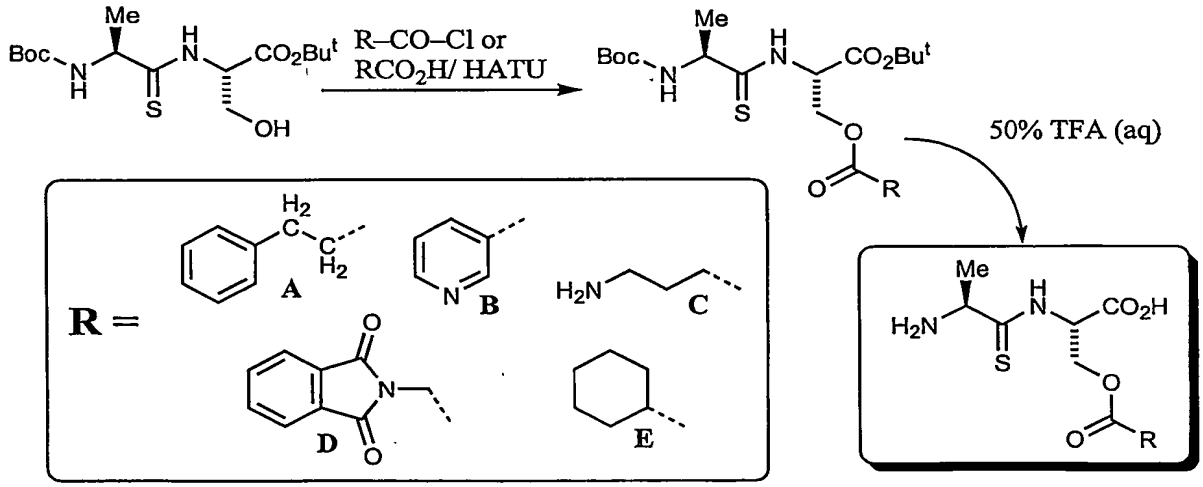


Figure 5

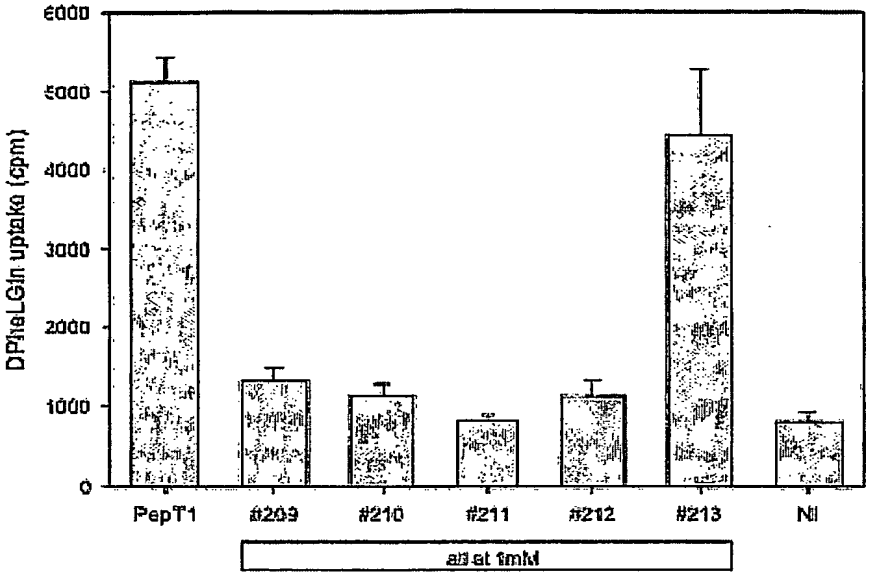

6000
5000
4000
3000
2000
1000
0
DPheLGln uptake (cpm)
PepT1
#209
#210
#211
#212
#213
Nil
all at 1mM

Figure 6

Selected synthetic thiopeptide targets prepared as drug carrier models

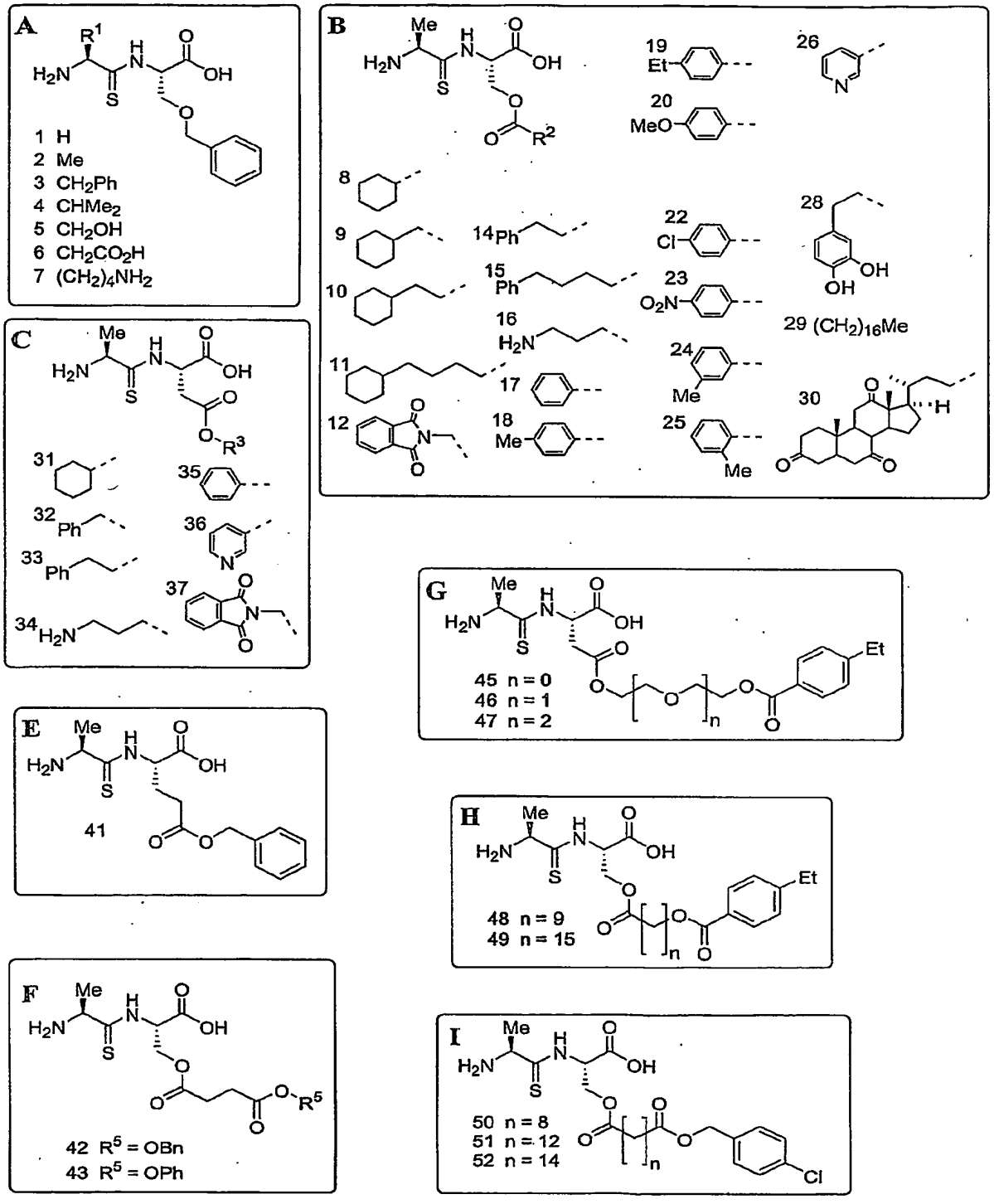


Figure 7

Entry	Type	Binding K_i/mM	Transport (*cf* Gly-Gln)†
1	A	1.41	
2	A	0.29	
3	A	0.37	
4	A	0.09	
5	A	0.34	<
6	A	0.53	
7	A	1.05	
8	B	0.3	=
9	B	0.2	=
10	B	0.12	=
11	B	0.11	=
12	B	0.03	<
14	B	0.1	<
15	B	0.09	=
16	B	0.6	<
17	B	0.23	<
18	B	0.2	=
19	B	0.13	<
20	B	0.16	=
22	B	0.09	>
23	B	0.11	=
24	B	0.08	
25	B	0.12	=
26	B	0.36	<
28	B	0.05	=
29	B	n.d.*	<
30	B	n.d.*	=
31	C	0.61	
32	C	0.25	
33	C	0.09	
34	C	1.58	
35	C	0.19	=
36	C	2.32	<
37	C	0.93	
41	E	0.03	
42	F	0.09	<
43	F	0.15	=
45	G	0.24	>
46	G	0.07	>
47	G	0.22	=
48	H	1.3	=
49	H	4.69	=
50	I	0.15	>
51	I	2.5	
52	I	9.7	=

* 29B/30B are strong inhibitors (est. K_i < 1mM), but are too insoluble for accurate K_i determination.

† Efflux of radio-labelled D-Phe-L-Gln is a positive indication of active transport via PepT1 (although negative results do not necessarily mean that substrates are not transported). In these assays (see elsewhere for details), the dipeptide Gly-Gln (which is known to be transported) caused *ca* 30% of labelled D-Phe-L-Gln to remain in the oocytes; at the same concentration, substrates were assessed as:

< (measurable efflux, but less transport than Gly-Gln, with ≥50% of D-Phe-L-Gln remaining)
= (efflux similar to the effect of Gly-Gln – i.e. 25-50% of labelled D-Phe-L-Gln remaining)
> (more efflux than Gly-Gln – i.e. <25% of labelled D-Phe-L-Gln remaining)

Figure 8a

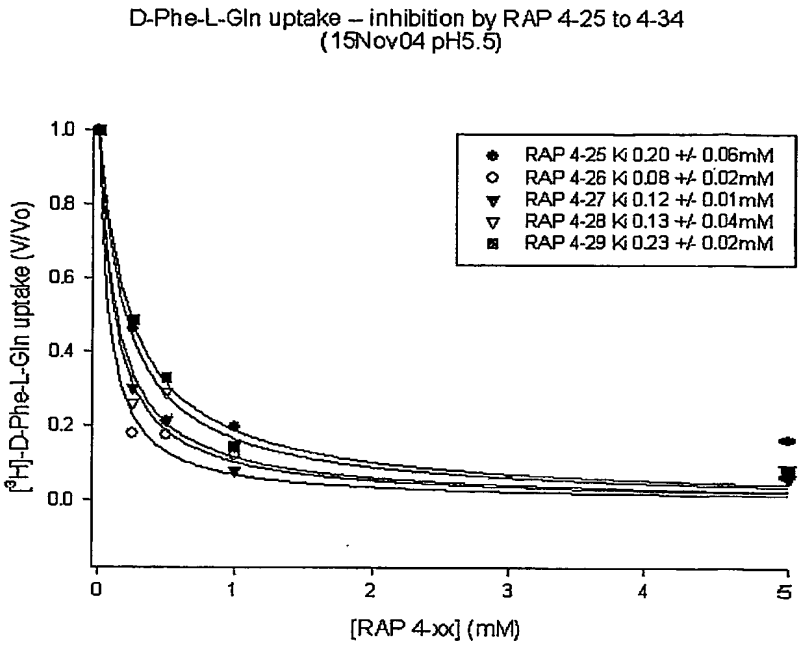


Figure 8b

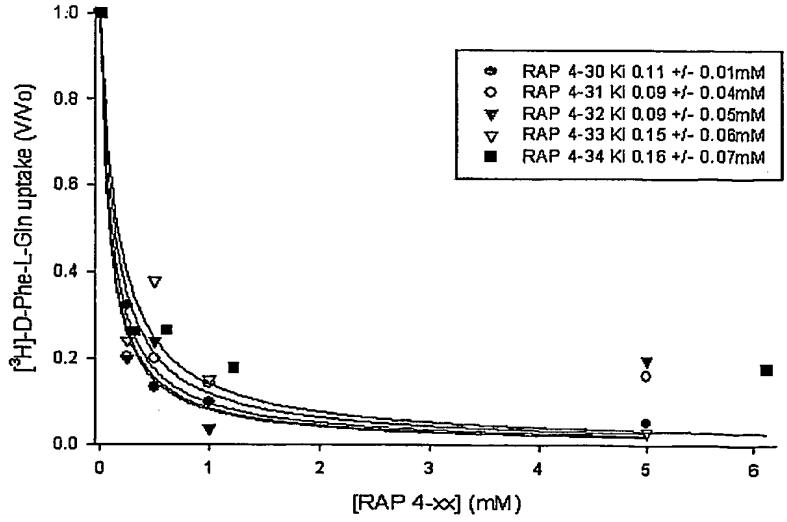


Figure 9a

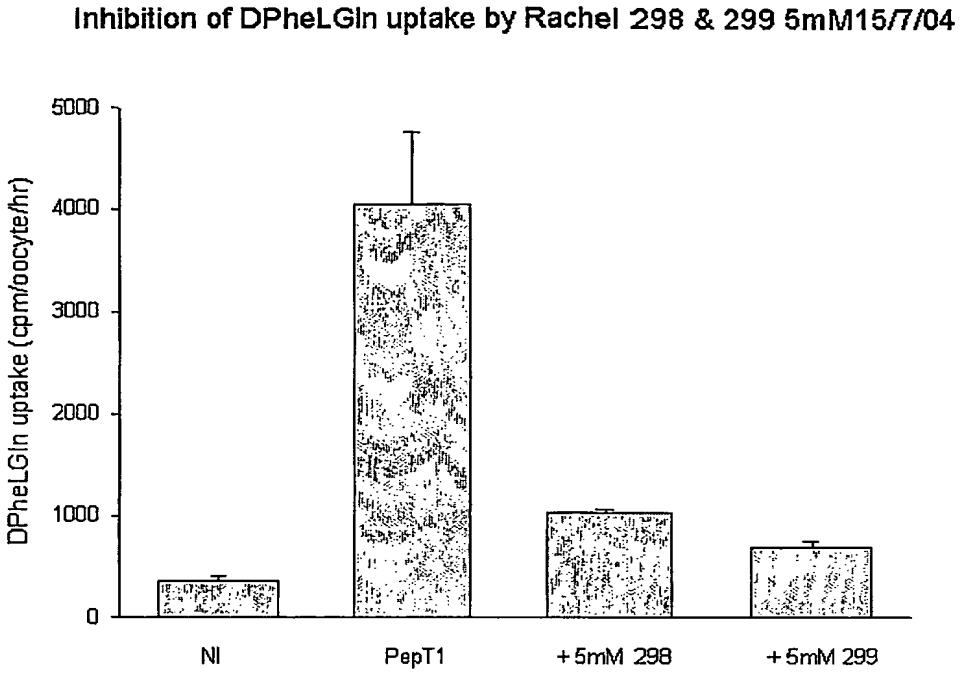


Figure 9b